

REMARKS

Applicants respectfully request reconsideration and allowance of this application in view of the following comments.

Claims 17-21 and 23 were rejected under 35 USC § 103(a) as being obvious over Wan et al. ("Wan"), *J. Immunol. Methods*, 162: 1-7 (1993), in view of Cubbage et al. ("Cubbage"), U.S. Patent No. 5,582,982.

Claim 22 was rejected under 35 USC § 103(a) as being obvious over Wan in view of Cubbage and further in view of Van Aken, U.S. Patent No. 5,489,537.

In response to *both* rejections, Applicants respectfully request that the Examiner reconsider and withdraw both rejections.

The Examiner states at the bottom of page 5 of the final rejection that:

"[T]here exist [in Wan] intracellular fluorescence which implies that the dye must have permeated the membrane of the cells at the bottom of the wells in order to fluoresce intracellularly."

Respectfully, this does not follow. Merriam-Webster's Online Dictionary defines "permeate" as "to pass through the pores or interstices of."

Wan is able to measure the intracellular fluorescence of the dye conjugated E. coli particles that have been *phagocytised* by Wan's cell. In other words, Wan is able to measure intracellular fluorescence *not* because the dye has permeated Wan's cells' membranes, but, rather, because the dye conjugated E. coli particles were *phagocytised*, i.e., taken up, internalized, by Wan's cells.

Wan measures the fluorescence of such internalized dye conjugated E. coli particles to give an indication of the phagocytosis process. Thus, Wan teaches in the abstract that "[t]he intensity of fluorescence associated with *intracellular* fluorescent particles was directly measured in the wells," and "[t]his assay provided a rapid and objective measurement of phagocytosis activity."

Thus, it should be clear that Wan is *not* measuring the intracellular fluorescence of *unconjugated* dye molecules. Rather, Wan *is* measuring the intracellular fluorescence of dye molecules *conjugated* to E. coli particles.

As this is completely different from what is required by the instant claims, Applicants submit that Wan in view of Cubbage alone or further in view of Van Aken does not make out a *prima facie* case of the obviousness of the present claims.

The Examiner also finds that because the claims use the open-ended terminology "comprising," they do not exclude substances attached to the dye, such as Wan's E. coli

particles. In response, Applicants submit that while it is true that the claims are open-ended, they are not so broad as to read on Wan's E. coli particles. Main claim 17 expressly requires that the "fluorescent dye is permeant to the membrane of a biological cell." Wan's fluorescent dye, because it is coupled to Wan's E. coli particles is not permeant to the membrane of Wan's cells. Instead, Wan's dye conjugated E. coli particles are expressly taught to be taken up by phagocytosis.

In view of the foregoing, Applicants respectfully submit that the Examiner would be fully justified to reconsider and withdraw both obviousness rejections. An early notice that both obviousness rejections have been reconsidered and withdrawn is earnestly solicited.

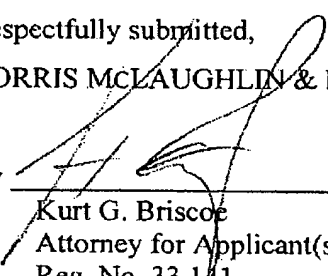
Applicants believe that the foregoing constitutes a bona fide response to all outstanding objections and rejections.

Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,
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By



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